

Boldi et al.

- 3 -

10/054,019

REMARKS

Claim 45 is the only claim pending in the application.

Claim 45 is currently amended.

Claim 45 is directed to a compound of formula (7'), and would be all the claims pending in the application if the instant amendment is entered.

Claim Rejection - 35 U.S.C. § 112

Claim 45 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner alleged that Applicant's previously amended Claim 45 filed on July 24, 2003, that excluded a compound described by Marsault et al. (see previous Office Action dated May 30, 2003) resulted in a claim that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner alleged that Applicants do not have support for the instant Markush group minus one specific compound.

Applicants respectfully traverse this rejection on the basis of a ruling in *In re Johnson*, 558 F.2d 1008, 194 U.S.P.Q. 187 (C.C.P.A. 1977). There the court stated:

"The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of §112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute. All that happened here is that appellants narrowed their claims to avoid having them read on a lost interference count." (194 U.S.P.Q. 196)

Applicants believe that *In re Johnson* stands for the proposition that it is improper to reject a claim to a genus minus a reasonable number of species within that genus, including species not specifically described in the specification, for lack of written description when the specification has adequate written description for the genus and species within that genus.

Baldi et al.

- 4 -

10/054,019

As previously amended, Claim 45 was a Markush claim directed to a genus minus a compound described in the art by Marsault et al. The Marsault et al. compound was the basis for a rejection of original Claim 45 under 35 U.S.C. 102 in a previous office action. Applicants' amendment and response filed on July 24, 2003, excluded the compound described in Marsault et al.

In this paper, Applicants have further amended Claim 45 to exclude additional species that were identified by the Examiner in the Office Action. Further, Applicants have amended Claim 45 to describe the excluded species by describing them in terms of their instant R^1 and R^3 groups of Formula (7') instead of by naming each excluded species. As currently amended, Claim 45 excludes the one species of Marsault et al. that was cited by the Examiner, two of the three species of Tronchet et al. that were cited by the Examiner, and the two species of Paulsen et al. that were cited by the Examiner in the §102 rejections (addressed below).

Applicants describe the genus of compounds of original Claim 45 (i.e., the genus without any species excluded) in the instant specification on page 41, at lines 17 to 23. Preparation and use of the compounds of original Claim 45 is described on page 51, at line 4, to page 54, at line 15.

Further, a number of species that fall within the genus of Claim 45 are described in Examples 2 and 3 of the instant specification as intermediates in the preparation of amides of Formula (Ib) and ureas of Formula (Ic), respectively. The compounds of Claim 45 that were used in the preparation of the compounds of Example 2 include compounds of Formula (7') wherein:

R^1 is benzyl and R^3 is N,N-diethylaminoethyl;

R^1 is benzyl and R^3 is 2-methoxybenzyl;

R^1 is 3-methoxy-benzyl and R^3 is butyl;

R^1 is methyl and R^3 is 2,4-dimethoxybenzyl;

R^1 is benzyl and R^3 is 3-methoxypropyl; and

Boldi et al.

- 5 -

10/054,019

R¹ is 3-methoxy-benzyl and R³ is 1-benzyl-pyrrolidin-3-yl.

Respectively, these compounds of Formula (7') have the following chemical names:

N'-(6-Benzyloxy-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl)-N,N-diethyl-ethane-1,2-diamine;

(6-Benzyloxy-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl)-(2-methoxy-benzyl)-amine;

Butyl-[6-(3-methoxy-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl]-amine;

(2,4-Dimethoxy-benzyl)-(6-methoxy-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl)-amine;

(6-Benzyloxy-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl)-(3-methoxy-propyl)-amine; and

(1-Benzyl-pyrrolidin-3-yl)-[6-(3-methoxy-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl]-amine.

The compounds of Claim 45 that were used in the preparation of the compounds of Example 3 include compounds of Formula (7') wherein:

R¹ is methyl and R³ is benzyl;

R¹ is methyl and R³ is 4-trifluoromethoxy-benzyl;

R¹ is 3-methoxy-benzyl and R³ is cyclopropylmethyl;

R¹ is methyl and R³ is 2-phenyl-ethyl;

R¹ is methyl and R³ is 2-(1H-indol-2-yl)-ethyl; and

R¹ is 3-methoxy-benzyl and R³ is allyl.

Respectively, these compounds of Formula (7') have the following chemical names:

Benzyl-(6-methoxy-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl)-amine;

Boldi et al.

- 6 -

10/054,019

(6-Methoxy-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl)-(4-trifluoromethoxy-benzyl)-amine;

Cyclopropylmethyl-[6-(3-methoxy-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl]-amine;

(6-Methoxy-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl)-phenethyl-amine;

[2-(1H-Indol-2-yl)-ethyl]-(6-methoxy-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl)-amine; and

Allyl-[6-(3-methoxy-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-d][1,3]dioxol-5-ylmethyl]-amine.

Applicants believe that the genus of original Claim 45 and the above-recited species are described in the instant specification in such a manner as to disclose to and teach those skilled in the art how to make and use the genus minus the one species of Marsault et al. that was cited by the Examiner. Accordingly, Applicants believe that the genus of Claim 45 minus the one species of Marsault et al. is patentable under 35 U.S.C. §112, first paragraph, and that the rejection is overcome.

Similarly, Applicants believe that the genus of Claim 45 minus the one species of Marsault et al. that was cited by the Examiner, two of the three species of Tronchet et al. that were cited by the Examiner, and the two species of Paulsen et al. that were cited by the Examiner is patentable under 35 U.S.C. §112, first paragraph. Accordingly, Applicants believe that currently amended Claim 45 is patentable under 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 U.S.C. § 102

- (a) Claim 45 remains rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Marsault et al. for reasons of record (the Examiner alleged that a particular species of Marsault et al. anticipates Claim 45).

Boldi et al.

- 7 -

10/054,019

Applicants respectfully traverse this rejection on the grounds that the particular species of Marsault et al. has been excluded from Claim 45. See Applicants' reasons given above for why Applicants believe that there is support for instant Claim 45.

(b) Claim 45 is rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Tronchet et al. The Examiner alleges that Tronchet et al. discloses compounds of Claim 45 wherein R¹ is methyl and R³ is methyl; R¹ is methyl and R³ is ethyl; and R¹ is methyl and R³ is phenyl.

Applicants respectfully traverse this rejection on the grounds that the species of Tronchet et al. wherein R¹ is methyl and R³ is methyl; R¹ is methyl and R³ is ethyl have been excluded from Claim 45 and that Claim 45 does not embrace the species of Tronchet et al. wherein R¹ is methyl and R³ is phenyl. See Applicants' reasons given above for why there is support for the genus of Claim 45 minus two of the three species of Tronchet et al. that were cited by the Examiner.

Regarding the species of Tronchet et al. wherein R¹ is methyl and R³ is phenyl, the Examiner correctly admitted that the instant specification describes on page 2, at lines 12-15, the term "cycloalkyl" as including a stable 3- to 7-membered monocyclic ring which is saturated or partially unsaturated (e.g., containing one or more double bonds). Respectfully, the Examiner then erroneously concluded that a 6-membered cycloalkyl that is partially unsaturated includes phenyl.

Phenyl is not a partially unsaturated cycloalkyl ring but is instead fully unsaturated. Partially unsaturated means that there is a part that is unsaturated, and thus there must be a part that is not unsaturated, i.e., a part that is saturated. A partially unsaturated cycloalkyl ring means that the ring has at least one carbon atom that is saturated (i.e., essentially sp³-like in character) and is capable of undergoing unsaturation (i.e., is capable of losing two protons on adjacent or distal atoms) to form a carbon-carbon double bond (i.e., wherein the carbon atom is essentially sp²-like in character). Examples of a partially unsaturated 6-membered cycloalkyl include cyclohexenyl,

Boldi et al.

- 8 -

10/054,019

cyclohexa-1,3-dien-1-yl, cyclohexa-1,4-dien-2-yl, and the like. Each of these groups has two saturated carbon atoms, which can each lose a proton to form a phenyl ring.

(Cyclopentadienyl is an example of a 5-membered, partially unsaturated cycloalkyl having one saturated carbon atom, which can, along with an exocyclic vicinal carbon atom, each lose a proton to form an exocyclic carbon-carbon double bond.) However, there is no saturated carbon atom in a phenyl ring, but instead all of the ring's atoms are involved in carbon-carbon double bonds (the electron densities of which are, of course, delocalized).

Accordingly, Claim 45 does not embrace the species of Tronchet et al. wherein R^1 is methyl and R^3 is phenyl, as R^3 in Claim 45 cannot be a phenyl group. This species of Tronchet et al. thus does not anticipate instant Claim 45.

(c) Claim 45 is rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Paulsen et al. The Examiner alleges that Paulsen et al. discloses compounds of Claim 45 wherein R^1 is benzyl and R^3 is $\text{CH}_2\text{CO}_2\text{CH}_2\text{CH}_3$; and R^1 is benzyl and R^3 is $\text{CH}_2\text{CH}_2\text{OH}$.

Applicants respectfully traverse this rejection on the grounds that the species of Paulsen et al. that the Examiner alleges anticipates Claim 45 has been excluded from Claim 45 for reasons given above.

In view of the amendment to Claim 45 and the above remarks, Applicants believe that Claim 45 is not anticipated by Marsault et al., Tronchet et al., or Paulsen et al., and is patentable under 35 U.S.C. § 102(b).

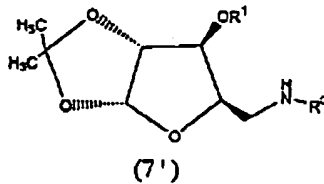
Claim Rejections - 35 U.S.C. § 103

Claim 45 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the combination of Marsault et al., Tronchet et al., Paulsen et al., as discussed above and Akhtar et al. in column 5, at lines 22-58. The Examiner alleges that the references disclose the following compounds of Formula (7') as follows:

Boldi et al.

- 9 -

10/054,019



(a) Marsault et al.:

 R^1 is benzyl and R^3 is isopropyl;

(b) Tronchet et al.:

 R^1 is methyl and R^3 is methyl; and R^1 is methyl and R^3 is ethyl;

(c) Paulsen et al.:

 R^1 is benzyl and R^3 is $\text{CH}_2\text{CO}_2\text{CH}_2\text{CH}_3$; and R^1 is benzyl and R^3 is $\text{CH}_2\text{CH}_2\text{OH}$;

(d) Akhtar et al.:

 R^1 is heptyl and R^3 is heptyl (reference formula (Ib)); R^1 is heptyl and R^3 is 3-dimethylaminopropyl (reference formula (Ic)); R^1 is dodecyl and R^3 is 3-dimethylaminopropyl (reference formula (If)); R^1 is decyl and R^3 is 3-dimethylaminopropyl (reference formula (Ih)); R^1 is heptyl and R^3 is hexyl (reference formula (Ii)); and R^1 is pentadecyl and R^3 is 3-phenylpropyl (reference formula (Ik)),

The Examiner further alleges that the above-identified art compounds essentially bracket the claimed compounds and this is the basis for the rejection. Applicants note that there are other compounds of Akhtar et al. in column 5, at lines 22-58. These other compounds are not identified above as compounds of Formula (7') because either they are linked via an oxygen atom instead of a nitrogen atom at position-6 or because they are tertiary amines at position-6 of the reference xylofuranoses whereas the compounds of Formula (7') are secondary amines at that position.

Boldi et al.

- 10 -

10/054,019

Applicants traverse this rejection on the grounds that not all of the limitations of Claim 45 are taught or suggested by the cited art (i.e., the above-identified art compounds do not essentially bracket the claimed compounds) and, thus, a *prima facie* case of obviousness has not been properly established. There are three requirements for establishing a proper *prima facie* case of obviousness:

- (1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;
- (2) There must be a reasonable expectation of success; and
- (3) The prior art must teach or suggest all the claim limitations.

Applicants believe that the cited art does not teach the limitations of Claim 45 wherein R³ is -(CH₂)₀₋₂-cycloalkyl, -C₂₋₆alkenyl, -(CH₂)₀₋₄-heterocycloalkyl, -(CH₂)₁₋₄-heteroaryl or -(CH₂)₀₋₂-O-aryl. Nor would one of ordinary skill in the art, at the time the instant invention was made, have conceived of all of the missing limitations. The prior art isopropyl, methyl, ethyl, ethoxycarbonylmethyl, 2-hydroxyethyl, heptyl, 3-dimethylaminopropyl, hexyl, and 3-phenylpropyl groups at R³ do not teach or suggest to the skilled artisan the instant -(CH₂)₁₋₄-heteroaryl group, for example. The invention of Claim 45 must be considered as a whole. When considered as a whole, the compounds according to Claim 45 cannot properly be considered to be obvious because the combination of Marsault et al., Tronchet et al., Paulsen et al., and Akhtar et al. does not teach or suggest to the skilled artisan all of the limitations of the claim.

Accordingly, Applicants believe that Claim 45 is nonobvious in view of the combination of Marsault et al., Tronchet et al., Paulsen et al., and Akhtar et al., and, thus, patentable under 35 U.S.C. § 103(a). Applicants request removal of Marsault et al., Tronchet et al., Paulsen et al., and Akhtar et al. as grounds for rejection under 35 U.S.C. § 103(a).

Boldi et al.

- 11 -

10/054,019

Conclusion

In view of the above amendment and remarks, Applicants believe that the rejections have been overcome. Applicants respectfully request removal of the rejections and reconsideration of Claim 45.

The Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment, to deposit account number 23-0455.

The undersigned would welcome a telephone call from the Examiner to discuss any matters related to this case that the Examiner thinks are amenable to resolution by such discussion.

Respectfully submitted,

Date: January 26, 2004

Claude F. Purchase, Jr.
Claude F. Purchase, Jr.
Reg. No. 47,871
Warner-Lambert Company LLC
2800 Plymouth Road
Ann Arbor, MI 48105
Tel. (734) 622-1692
Fax (734) 622-1553